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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/863,823 | 05/23/2001 | D. Wade Walke | LEX-0180-USA | 8988 |

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| EXAMINER | |
|---|---|
| HAMUD, FOZIA M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1647 | |

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | *09/863,823* | WALKE ET AL. | |
| | Examiner | Art Unit | |
| | Fozia M Hamud | 1647 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 22 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *22 August 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-4, 6-13*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10.☐ Other: _____

## ADVISORY ACTION

1. Receipt of Applicants' amendment and arguments, filed on 22 August 2003, is acknowledged. Claim 2 has been amended. Claim 5 has been previously canceled. Thus claims 1-4 and 6-13 are pending and under consideration.

2. The following previous rejections and objections are withdrawn in light of Applicants amendments filed on 22 August 2003.

(I) The rejection of claim 2, made under 35 U.S.C.§ 112, second paragraph.

***Response to Applicants' Arguments:***

**Claim Rejections - 35 U.S.C. § 101/112**

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3a. Claims 1-4 and 6-13 stand rejected under 35 U.S.C. § 101, for reasons of record, set forth in the office action mailed on 09/25/02, pages 4-8 and reiterated in the office action mailed on 05/19/03, pages 2-7, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

**I.** Applicants argue that the instant invention has a number of substantial and credible utilities, not the least of which is in **forensic** analysis. Applicants point out that the use of the presently described polymorphisms in forensic analysis does not require the identification of a specific medical condition, but to

distinguish individual members of the human population based on the presence or absence of one or both of the described polymorphisms. In the worst case scenario, each marker is useful to distinguish 50% of the population, thus, the ability to eliminate 50% of the population from a forensic analysis is clearly a real world, practical utility.

II. Applicants further argue that if each and every invention were required to have a unique utility, the Patent and Trade Mark office would no longer be issuing patents on batteries, automobiles, golf balls and treatments of a variety of diseases. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions. Applicants cite in re Brana, and contend that "the Office is confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". Applicants argue even if further research might be required in certain aspects of the instant invention, this does not preclude a finding that the invention has utility, because courts have stated that "pharmaceutical inventions, necessarily includes the expectation of further research and development". However, the need for some experimentation does not render the claimed invention unpatentable. Applicants further submit that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have a reason to doubt the objective truth of such statement.

III. Applicants argue that the Examiner's response to the Applicants argument that the claimed nucleic acid could be used in high through-put DNA chips, is flawed, because firstly, expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip, rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels of two or more particular tissue types. Second, the particular cell types and controls in which the expression levels are assessed directly indicate to the skilled artisan whether "the polynucleotide expression should be increased or decreased". Also, the skilled artisan already have used and continue to use sequences such as Applicants in gene chip applications every day, without any information about the polynucleotide or the encoded protein. It defies logic that skilled artisan would waste money and time by including such sequences on gene chips if they did not yield any useful information. Furthermore, Applicants contend that only the assertion of one credible utility is needed to meet the requirement of under 35 U.S.C.§ 101.

IV. Applicants also argue that another specific utility for the claimed nucleic acids is in "identification of coding sequence" and "mapping a unique gene to a particular chromosome". Applicants argue that the claimed nucleic acids have utility not because they can be used to produce the encoded protein, but because they provide biologically validated empirical data, that specifically define that portion of the corresponding genomic locus that actually encodes exon sequence. Also, significant is the claimed sequences define how encoded exons are actually spliced together to produce active transcripts. Thus Applicants

submit that the practical scientific value of biologically validated, expressed, spliced and polyadenylated mRNA sequences is readily apparent to those skilled in the art. Applicants also argue that the claimed nucleic acids provide exquisite specificity in localizing the specific region of human chromosome 17 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. Applicants state that Venter et al demonstrates the significance of expressed sequence information in the structural analysis of genomic data.

V. Finally Applicants argue that the current rules and regulations regarding the examination of patent application is and always has been as set forth in 35 U.S.C . and patent rules as set forth in 37 C.F.R, and not the manual of patent examination procedures or particular guidelines for patent examination. Furthermore, Applicants submit that it is the job of the judiciary and not the USPTO to interpret these laws and rules. Again applicants cite various new patents that were recently issued, and contend that it is capricious and arbitrary to hold the instant Applicants on a different standard.

Applicants' arguments have been fully considered but are deemed unpersuasive.

With respect to Applicants' first argument, using the claimed nucleic acids for forensic analysis to distinguish individual members of the human population based on the presence or absence of one or both of the described polymorphisms does not afford the claimed nucleic acids specific and substantial utility, because Applicants have not disclosed the significance of the presence of

the claimed nucleic acid in a subject. The mere presence or absence of the claimed nucleic acid in a subject is not substantial utility, because any DNA can be used for said general purpose. In order for the presently claimed nucleic acid to be useful in forensic analysis, it must provide significant information about an individual, other than that it is either present or absent in said individual. There is no doubt that SNP research is a significant and emerging field. For example, the presence of a specific SNP can be used to identify those individuals who are likely to benefit from a new medication, from those who could suffer adverse side effects or to determine the optimal dosage. However, in the instant case, Applicants have not shown that the claimed nucleic acid can be used in any meaningful way, other than that it may distinguish 50% of the population as having it. Does this mean that those individuals that have it: are susceptible to certain diseases, are unique and can be solely identified because of the presence of said DNA?

With respect to Applicants' second argument, while each and every composition does not have to be unique in order for it to be patented, it has to have a specific and substantial utility. The skilled artisan must know how to use said composition. Novel golf balls, automobiles and batteries must provide a useful improvement over already existing golf balls, automobiles and batteries, in order to satisfy the requirements under 35 U.S.C.§ 101. Although the need for further research does not necessarily equate for lacking utility, however, in the instant case, Applicants have not provided one single specific and substantial utility for the claimed nucleic acid, other than general uses that are applicable to

all DNAs. As was addressed in previous office actions, in re Brana, 34 USPQ 1436, 1441 (Fed. Cir. 1995), disclosed compounds with specific structure and specific activity. Thus, in that case evidence of success in structurally similar compounds was relevant in determining whether one skilled in the art would believe an asserted utility; therefore, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement. Furthermore, in re Brana, there were test results showing that several compounds within the scope of the claims exhibited significant antitumor activity against standard tumor model in vivo. However, instant Applicants do not provide an activity for the proteins encoded by the claimed nucleic acid, nor do they provide the physiological significance of these proteins, only, an assertion that the proteins of the instant application can be used in forensic analysis.

With respect to Applicants' third argument, although the knowledge of the function of a particular nucleic acid may not be necessary for said nucleic acid to be used in a gene chip, however, the significance of the altered levels or forms of a gene in a tissue compared to another tissue, must be known. Furthermore, Applicants' have not disclosed those conditions or reasons in which it might be desirous to increase or decrease the claimed nucleic acid. Therefore, following the expression levels of a nucleic acid without the knowledge of the conditions and circumstances that would lead the skilled artisan to increase or decrease it, would be meaningless. Finally, evidence of commercial success, while sometimes persuasive as secondary evidence of non-obviousness, is immaterial to utility and enablement. Many products have enjoyed commercial success due

to fads or clever advertising, wherein the products would not have met the legal standards for utility and enablement.

With respect to Applicants' fourth argument, using the claimed nucleic acid a chromosomal marker does not provide the claimed invention a specific utility, because no meaningful information will be obtained from tracking the level of expression of the claimed nucleotide, because there is no physiological or biological significance attached to these nucleotides or the encoded proteins. Without a disclosure of a particular disease state in which the claimed nucleic acid are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression monitoring assay mean. For example, if a compound is tested on a microarray comprising the claimed nucleic acid and affects expression of the nucleic acid negatively, it cannot be determined if that means that the compound is a potential good drug for a disease or would acerbate the disease if administered. The test results also would not have meaning in terms of what specific disease is relevant. The relevance of Applicants' citation of Venter et al (Science Vol.291, pages 1304-1351, 2001) is not clear. Venter's reference is about decoding and sequencing the human genome. Venter discloses that only 1% of SNPs results in variation in proteins, and that the task of determining which SNPs have functional consequences remains an open challenge, (see abstract). Therefore, since Applicants have not disclosed the physiological relevance of the claimed nucleic acid, one of ordinary skill in the art would not know how to use it.

Furthermore, the fact that the claimed nucleic acid encodes a sequence and can be used to identify how exons are actually spliced together to produce active transcript, does not provide the claimed nucleic acid a specific and substantial utility. Instant claims are drawn to nucleic acid molecules, not methods of specifically defining portions of a gene that actually encodes a sequence. Finally, Applicants are correct in that the assertion of one credible utility is needed to meet the requirement under 35 U.S.C.§ 101, however, said utility must also be specific and substantial (real world use). The instant case fails to disclose a specific and substantial use for the claimed nucleic acid, because there is no biological significance nor correlation to a specific disease state attached to said nucleic acid.

With respect to Applicants' fifth argument, the Examiner is only applying and enforcing the requirements under 35 U.S.C.§ 101, which requires that an invention must not only be novel but must also be useful. The contents of 35 U.S.C, 37 C.F.R, judicial decisions, and guidelines established by the USPTO are not subject to examiner review and will not be questioned or defended by the Examiner. These decisions made by legally empowered government entities to which the Examiner is subordinate and those decisions will be followed without question by the examining corps. Finally, Applicants are reminded that each Patent Application is examined on its' own merits and each Patent Application must meet the criteria set forth in the Revised Interim Utility Guidelines, for a specific and substantial credible asserted utility, or a well established utility.

3b. The claimed invention stands rejected under 35 U.S.C. 112, first paragraph, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Conclusion***

4. No claim is allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
05 February 2004

Gary L. Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
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Continuation of 3. Applicant's reply has overcome the following rejection(s): The rejection of claim 2, made under 35 U.S.C.§ 112, second paragraph.